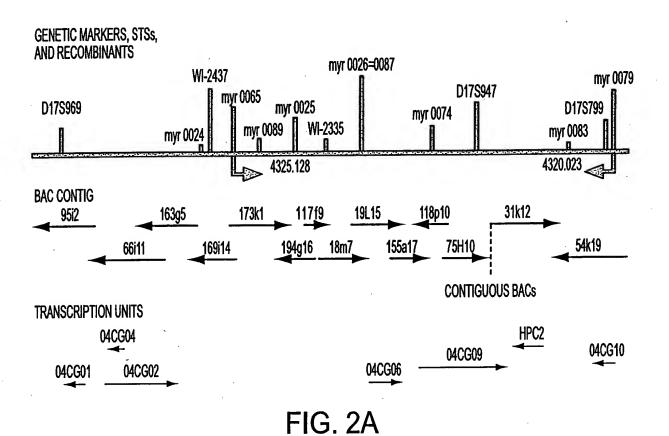


FIG. 1



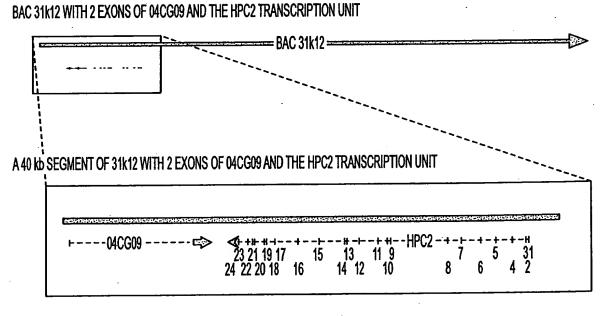


FIG. 2B

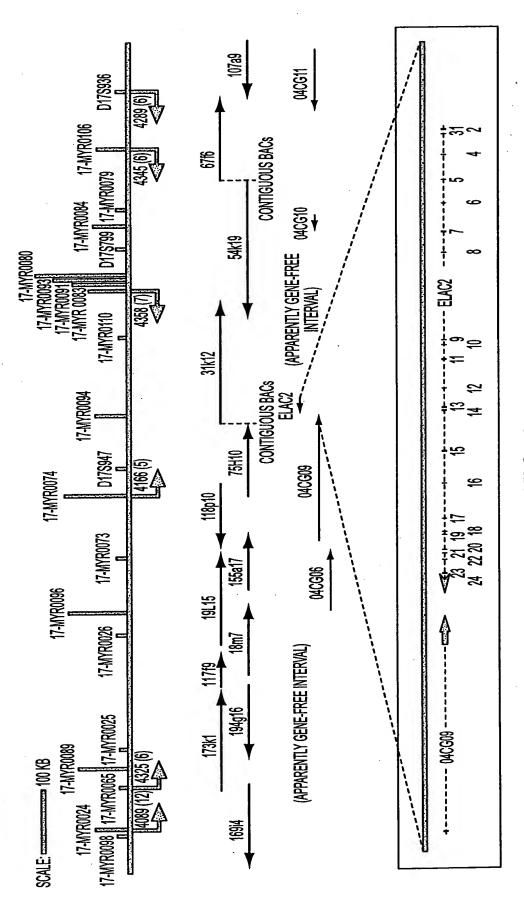


FIG. 3

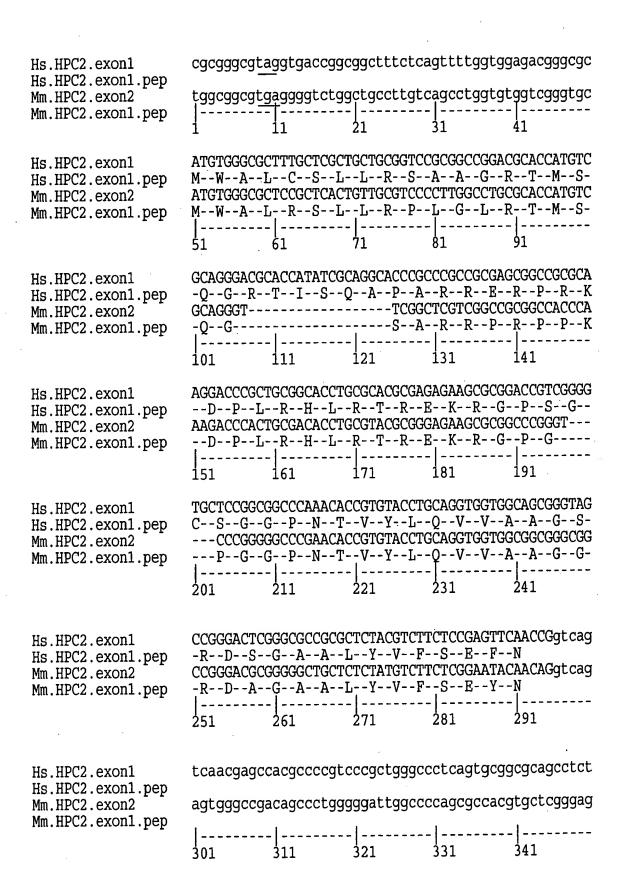
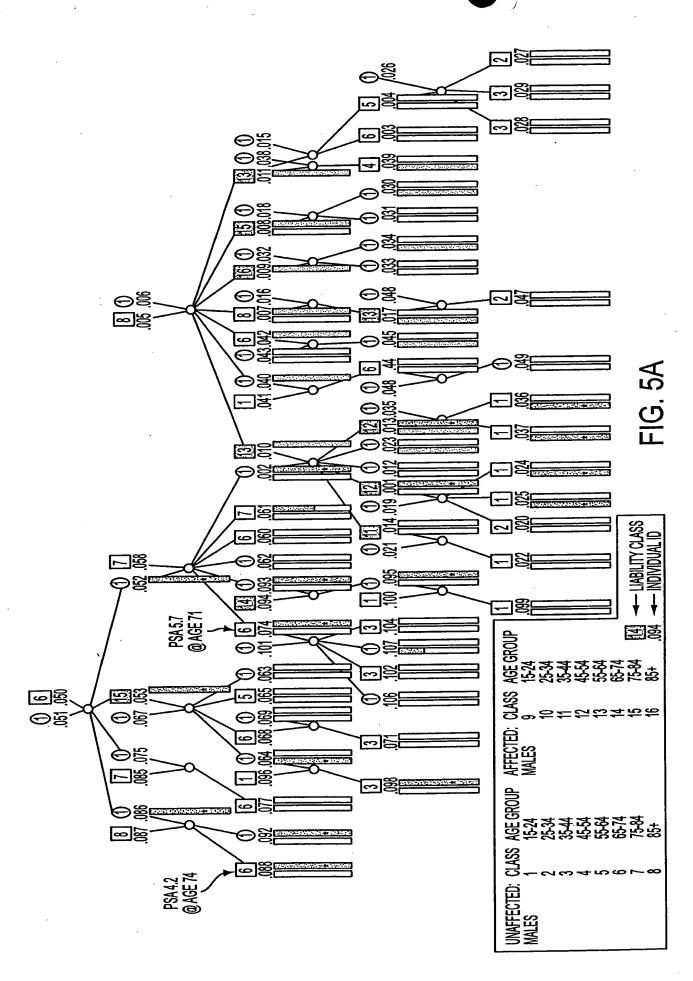
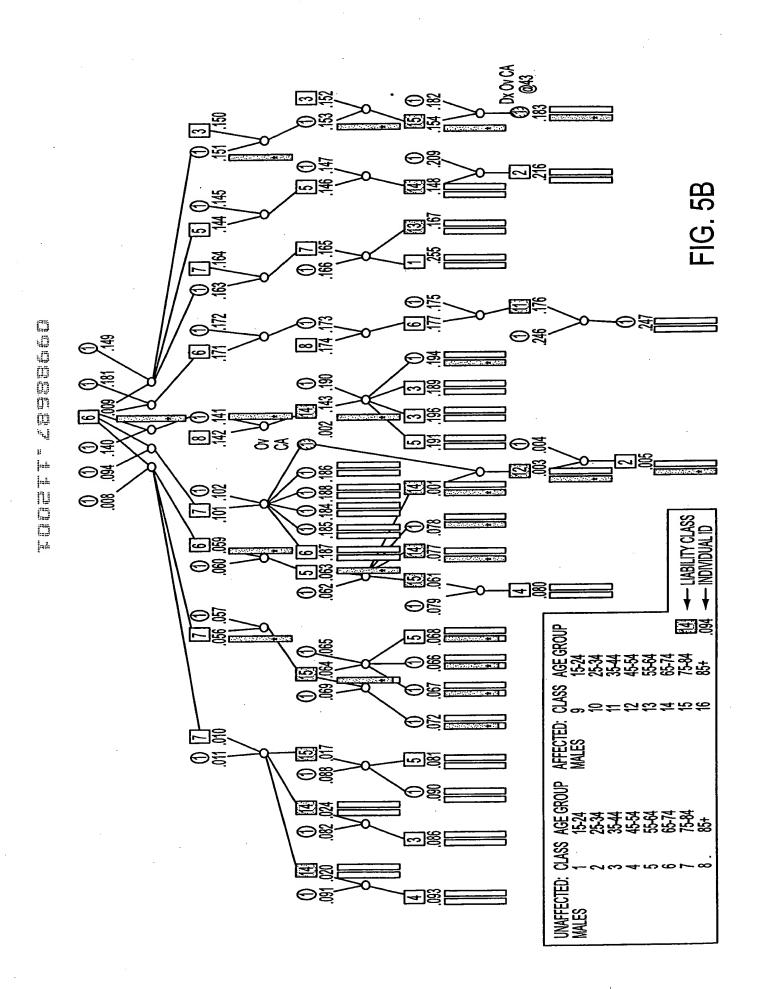


FIG. 4





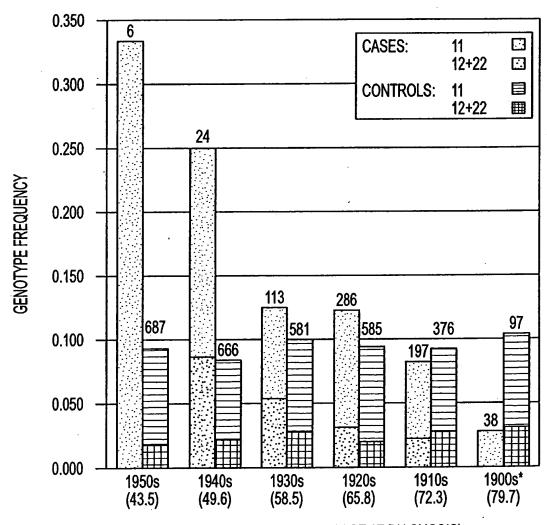
MWALCSLLRSAAGRTMSQGRTISQAPARRERPRXDPLRHIRTREKRGPSGCSGGPNTVYLQVVA MWALRSLLRPLGLRTMSQG·····SARRPRPSKDPLRHIRTREKRGP··GPGGPNTVYLQVVA MKMLFFGIKVSRHLISSTSCLFKDNNEELLESIKERIARNRRILQKHSSSHLKAREVNASISNLRQSMAAVQKKQKAAHEPPANS·IVNIPSQVSIEVUG MENNEATNGSKSSSNSFVFNKRRARGFDITDKKKRNLERKSQK·LNPTNTIAYAQILG MFTFIFFITH	AGSRDSGAALYWFSBFNR··YLFNCGEGVORLMOB AGGRDAGAALYWFSBYNR··YLFNCGEGVORLMOB N·GTGLLRACFILRTPLKT·YMFNCPENACRFLWO TGMDTQDTSSSWLLFFDKQRFIIFNAGEGLQRFCTE PTSDTKHPLLLWQSAHGEKYRRGKIGGEGSORSLTE	SSGPLKGIELAVRPHSAPEYEDBETMTWYQIPIHSEQRRGKHQPWQSPERPLSRLSPERSSDSESNENEPHLP YOUNGESTED BLAVRPHSAPEYKDBTMTWYQVPIHSERRCGKQQPSQSPRTSPNRLSPKQSSDSGSAEN-GQCPPE ANYHTRSFGPSTPDPIVLVNDEVVKISAIIPYTMENYEDAGLKWTYIPLKP.CHSEDSGSNKSGD ANYHTRSFGPSTPDPIVLVNDEVVKISAIIPYTMENYEDAGLKWTYIPKMFPKHAPTDRYDPS&DPHLN		1 ILPICENATRORIOGKADAPVALVINIMAPASIVLVDSRIYQQW MBRIRGPDTQ. HLVLINENCASVHNL. RSHKIQTQLINLIHPDIRPLL 1 ILPICENDTRKRYQARTDAPVALAVHIJAPESIVLIDSRYQQW MBRIRGPDTQ. HLILINENCPSVHNL. RSHKIQTQLISLIHPDIRPQL 2 VKALLIDSSSLQPIRLNGEKQLDYMVHISDDAVINTPTIVRL MBKILINNPSITHLLINGGNPVIPAVESVYKHTRLLIRSIAPSLIFPAL 3 VKALLIDSSSLQPIRLNGEKQLDYMVHISDDAVINTPTIVRL MBKIRINL.TQ. HILLAGHQRPLLIIVSHQKTVRKNMARPILKASSRIAA 4 OABLIFSLKSLESYYSSPDEQTIGAKPVNCILHILSPSSVTSSPTYQSW MKKIRIL.TQ. HILLAGHQRPLPLIIVSHQKTVRKNMARPILKASSRIAA 5 LINARVEKFKDYDCA.ELGWYYFLGDBYTTINDNLEAFIDIRBKNNYGKYNH MISHNKISPNTISPFGSALTTLKLKALLOV.NNYHLBKTDRVFSKDF
ਜਜਜਜ ,	65 57 100 58 58	155 147 193 156 108	226 219 238 203 203	317 313 322 280 266
ELAC2 Elac2 CE16965 gi6850339 YKR079C	ELAC2 Elac2 CE16965 gi6850339 YKR079C	BLAC2 Blac2 CE16965 gi6850339	BLAC2 Blac2 CB16965 gi6850339 YKR079C	BLAC2 Elac2 CE16965 gi6850339 YKR079C
(HSA) (MMU) (CEL) (ATH) (SCE)	(HSA) (MMU) (CEL) (ATH) (SCE)	(HSA) (MMU) (CEL) (ATH) (SCE)	(HSA) (MMU) (CBL) (ATH) (SCR)	(HSA) (MMU) (CEL) (ATH) (SCE)

FIG. 6A-2

FIG. 6B-1

674 VRMGK. DATILLIHBATILEDGI	ATLIDITM	751 KWORODRPTMPKLIRPLKALRAGDI BBMBERRBKRELRQVRAALLSRELAGGLEDGEPQQKRAHTBEPQAKKVRAQ 747 KWORODRPTVPKLIRPLKALRAGDI BBMVERRBKRELRLVRAALLITQQ·ADSPEDREPQQKRAHTDEPHSPQSKKESVANTLGARV 794 RWRRDHEDPLVSKLLIPIRRBWRVABL FBLTIKKBQRVLKDKELSEKRGQLKA	SINMADLHVLPKVLPYRKTLRRDEMVEDEDADDVAMDDLKEBAL I LVDDYRKIGEQQRIFPLLAKARVEKEBEDVDDVESVQDLEVKLKKHKKN	DO DO BENTON BENEVISIPIKK NOP - TVPNV	(Syn sp)gi2500943 300 RDR LTVRIPRRTADPAIAMSTPQASPA (Me_t)gi2622965 291 DDL MTVRVKAYDSSPDS
674 670 699 717 708	226 226 219 215	751 747 794	794	344	3 300 291
(HSA) BLAC2 (MMU) Blac2 (CEL) CB16965 (ATH) gi6850339 (SCE) YKR079C	(Rs_c)elac (Syn_sp)gi2500943 (Me_t)gi2622965	(HSA) ELAC2 (MMU) Elac2 (CEL) CE16965	(ATH) gi6850339 (SCE) YKR079C	(HSA) BLACL (Bs c)elaC	(Syn_sp)gi250094 (Me_t)gi2622965

FIG. 6B-2



DECADE OF BIRTH (AVERAGE AGE AT DIAGNOSIS)

FIG. 7

1920s - 1950s CASES		ONTROLS		
	OBSERVED	•		
	CASES	CONTROLS		
00, 01, 02	372	139		
11, 12, 22	57 (13.3%)	9 (6.1%)	ODDS RATIO	2.4
			P-VALUE	0.026
00, 01, 11	387	143		
02, 12, 22	42 (9.8%)	5 (3.4%)	ODDS RATIO	3.1
			P-VALUE	0.022
00, 01	347	137		
02, 11, 12, 22	82 (19.1%)	11 (7.4%)	ODDS RATIO	2.9
	<u> </u>	 	P-VALUE	0.001
1920s - 1950s CASES	OVO DEDICDEE UN	AECECTEDS		
19208 - 19308 CASES	S VO. PEDIGNEE UN	AFTECTEDS		
00, 01, 02	372	2151		
11, 12, 22	57 (13.3%)	220 (9.3%)	ODDS RATIO	1.5
*	<u> </u>		P-VALUE	0.013
00, 01, 02	372	2151		
11	40 (9.3%)	170 (7.2%)	ODDS RATIO 11	1.4
12, 22	17 (4.0%)	50 (2.1%)	ODDS RATIO 12,22	2.0
14,44	17 (1.070)	00 (2,0/	P-VALUE	0.017
			TREND STATISTIC	8.09
			P-VALUE	0.004

FIG. 8

1 MASSSISLKARROPISKARROPISKARRORSCULLERKORITHINGGERGGLEGNOALDY-IDLIDARGIDLELINGERGERGGRUNGGERGERGERGERGERGERGERGERGERGERGERGERGER	TISUVILDANHCPGAIIIMLFORFLATT
CPSF73 family (HSA) CPSF73 (ATH) gi6751699 (SCB) YSH1 (Syn sp) gi2496795 (Me_t) gi2622312 1 (ATH) gi2979557 (ATH) gi2979557 (ATH) gi2979557 (ATH) gi6850339 (ATH) gi6850339 (ATH) gi6850339 (ATH) gi6751699 (SCB) YKR079C (ATH) gi6751699 (SCB) YKR079C (SCB) YKR079C (SCB) YKR079C (SCB) YKR079C (SCB) YKR079C (ATH) gi6751699 (SCB) YKR079C (ATH) gi6751699 (SCB) YSH1 (SYn sp) gi2496795 (SCB) YSH1 (SYn sp) gi2496795 (SCB) YSH1 (SYn sp) gi2622312 (SYn sp) gi2622312 (HSA) ha3611	PS02

FIG. 9-1

634 ···LEBFQTCLWRHCKHAFGCALVHT·····SGWKWWYSGDTMP·CEALVRMGK······DATLLTHBATTLBDGL······ 667 ···LNDLISPWWHCPQAYGVVIKAABRVNSVGRQILGWKMWYSGDSRP·CPRTVBASR······DATILITHBATTRBDAL······ 660 ···IRYRQTCRAINCDWAYSNSITFR···MDRNNBHNTFKWSNSLBIGY······NSDLLITHBATTLBNQL·····	232 ···RGGRGLIPVRALGRAQBLLLILDBYWQNHP···BLH··DIPINY ·· 387 388 ·· VDYIISRSAMTDYQQTSBRIRAL ·· KPPHVIILVMGBANBMRLKQK 242 ···QGGRVLIPPRALGRAQBLLLILDBYWANHP···DLH··NIPINY ·· 397 398 ·· VHYIISRSAMADYAQTSTRLKBL ·· MPPNIILIVMGBANBMRLKQK 237 ···RGGRVLLPVRALGRAQBIMLILDBYWSQHAD ·· BLGGGQVPIRY ·· 399 400 ·· VBBISRAAMVDPQBNLBRIRKII ·· SAPNIILIVMGBANPMGRLKSA 216 ··· KGRNILLPVPPLGLAQBILKLLRTHH······ QFTGRQVNLMA ·· 359 360 ·· LBDYLLADBSDGRNTTQLIHNL ·· RPQHLVMVHGQPSDIBDLTSL 407 ··· RGGKILIPVFAVGRAQBLMIVLBRYRTGIIDBVPVYIDGMIMR ·· 570 571 ·· KTIRGFSGHSDRRQLMRYKRISPKPRILLICHGDNYKTLDLASS	870 ···PHALVÜCGTYSTGK·EKÜFLATADVLGSKVGMSQEKYKTLQCLN··985 986··IYGTPÜSEHSSYLEMKRFVQWIL··KPQKITTPTVNVGTWKSRSTME 567 ···PKTLFILIGSYTIGK·ERLFLEVARVLREKIYINPAKLKLLECLG··685 686··RYEWPYSEHSSFTELKRFVQKV··SPEVITIPSVNNDGPDSAAAMV 433 ···YRVLFLVGTYTIGK·EKLAIKICEFLKTKLFVMPNSVKFSMMLT··602 603··VFNVPPYSEHSSFNDLVKFGCKL	693 694 · EEBRAVEKTHSTITSQAISVGMAM · NAEFIIMINHESQR · YAKIVPLF · · · · · · · · · · · · · · · · · · ·
BLAC2 family (HSA) BLAC2 (ATH) gi6850339 (SCB) YKR079C	CPSF73 family (HSA) CPSF73 (ATH) gi6751699 (SCE) YSH1 (Syn_sp) gi2496795 (Me_t) gi2622312	PSO2 family (HSA) ha3611 (ATH) gi2979557 (SCB) PSO2	BLAC2 family (HSA) BLAC2 (ATH) gi6850339 (SCB) YKR079C

%GAP (HSA) ELAC2

FIG. 10

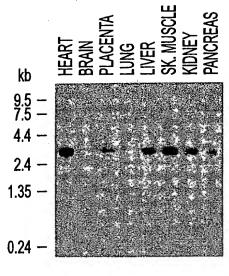


FIG. 11A

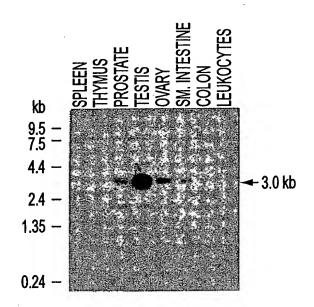


FIG. 11B



FIG. 11C



FIG. 11D

•		
Sequences 52 SGGPNTVYLOVVAAGSRDSGAALYVFSERNRYLFNCGEGVQRLMQEHKLKVARLDNIFLTR.MHWSNVGGLSGMILTLKKE 44 PGGPNTVYLQVVAAGGRDAGAALYVFSELNRYLFNCGEGVQRLMQEHKLKVARLDNIFLTR.MHWSNVGGLCGMILTTLKE 87 VNIPSQVSIBVLGN.GTGLLRACFILRTPLKTYMFNCPENACRFLWQLRIRSSVVDLFITTS.ANWDNIAGISSILLIS.KE 87 VNIPSQVSIBVLGN.GTGLLRACFILRTPLKTYMFNCPENACRFLWQLRIRSSSVVDLFITTS.ANWDNIAGISSILLIS.KE 86 VNIPSQVSIBVLGN.GTGLLRACFILRTPLKQRFITENAGRGLQRFCTEHKIKLSKIDHVFLSR.VCSETAGGLPGLLLTLAG 87 VNIPSQVSIBVLGNDTQDTSSSVLLFFDKYFFGKIGEGSQRSGTEHKIKLSKIDHVFLSR.VCSETAGGLPGMILTIAG 88 VNIPSQVSIBVLGTGMDTQDTSSSVLLFFDKYFFGKIGEGSQRSGTEHKIKLSKIRDIFLTGRUNMSDIGGLPGMILTIAD	region 475 RKRSQYPBİİRİLĞIĞSAIPMKIRNVSATLİVNISPDTSİLLİDÇĞBĞTRĞQİLÇRHYĞDQ.VDRVLGTLİAAVEVSH.LHADHHTĞLİPSİLLİQRERR 471 BKRSQYPBİİRİRİĞIĞSAIPMBIRNVSSTLİVNLSPDKSVLLDÇĞBĞTRĞQİLÇRHYĞQQ.IDRVLÇSLTAVEVSH.LHADHHTĞLİNTILLIRRKE 480 KMDCERPKLITERĞISSAVPSKYRNVTĞ.YLVBASBNSAİLLİDVĞBĞTYĞQMRAVFĞEDĞCKQLLVNILNCVILITH.AHQDHMNĞLIYTILARRKE 479 KIRRDDMBİVILLĞIĞSSQPSKYRNVSAIRIDLESRĞSİLLİDÇĞBĞTLĞQİLKRRYĞLDĞADBAVKLIRÇİNİSH.İHADHHTĞLİRRİLLARIKLALRSK 460 ABKKKHVBİİTLIĞIĞSALPSKYRNVVSTLİVKVPFTDADĞNTINRNİMLDAĞENTLGTLİHRMFSQLAVKSIFQDİLKMİYLİSH.LHADHHLĞTI SVLINBWYK	ELACI, N-terminal=His motif region (HSA) ELACI 1 MSNDVTREGGGAAYPSPTRGASAVVLRCEGRCWLFDCGRGTQTQLMKSQLKAGRITKIFITH.LHGDHFFGLPGLLCTTISL (ES_C) elaC 1 MKRDELMELIFLGTSAGVPTRTRNVTA.ILLNLQHPTQSGLWLFPDCGRGTQHQL (Syn_sp) gi2500943 1 MREVIRELGTSSGVPTRNRNVSS.IALRLPQRAELWLFPDCGRGTQHQFLRSEVKISQLTRIFITH.LHGDHIFGLMGLLASSGL (Syn_sp) gi2622965 1 MMEVTRIGGSAVPSKNRNHTS.IALRIPGEIFLEPDCGRGTQRQMALAGISPMKVTRIFITH.LHGDHILGTPSGRAF
ш 8 го 44 86 44	9 7 4 4 4 4	11=H
BLAC2, N-terminal sequences (HSA) BLAC2 52 SGGPN (MMU) Blac2 44 PGGPN (CEL) CEL6965 87 VNIPS (ATH) gi6850339 45 NPTNT (SCE) YKR079C 1 MF	ELAC2, His motif region (HSA) ELAC2 475 El (MMU) Blac2 471 El (CEL) CEL6965 480 Kl (ATH) gi6850339 479 Kl (SCE) YKR079C 460 A	<pre>BLAC1, N-terminal=Hi (HSA) BLAC1 1 (Es_c) elac 1 (Syn_sp) gi2500943 1 (Me_t) gi2622965 1</pre>
BLAC2, (HSA) 1 (MMU) 1 (CEL) (CEL) (ATH) (SCE)	BLAC (HSA (MMU (CBL (ATH (SCE)	BLAC (HSA (ES (Syn (Me

FIG. 12

